Remarks/Arguments

The present amendment amends claims 1 and 7, and adds new claims 20-25. The amendment is without prejudice to future prosecution.

Claim 1 was amended to indicate using caspase 3 activity as an indication of viral activity to measure virus stability and potency in either: (i) different formulations; or (ii) a single formulation at two or more time intervals. Claim 7 was amended to depend from claim 1 and focuses on a single formulation at two or more time intervals using language provided in claim 1. New claim 25 depends from claim 1 and focuses on different formulations. Support for the amendments to claims 1 and 7, and new claim 25, is provided, for example, on page 1, lines 23-26, page 12, lines 5-12, and original claim 7.

New claims 20-24 ultimately depend from claim 18. Claim 18 refers to either measles virus, mumps virus or rubella virus. New claim 20 indicates using caspase 3 activity as an indication of viral activity to measure virus stability and potency in different formulations. New claim 21 indicates using caspase 3 activity as an indication of viral activity to measure virus stability and potency of a formulation at two or more time intervals. New claims 22, 23 and 24 refer to claims 18, 20, or 21, and indicate the virus is either measles or mumps.

35 U.S.C. § 112, Second Paragraph (Definiteness)

Claims 1-8, 18 and 19 stand rejected as allegedly indefinite based on reference to "viral activity". The examiner argues that it is not readily apparent what type of viral activity is encompassed, for example potency, stability and/or ability to induce caspase 3; that applicants assertion concerning the specification not defining "viral activity" as viral stability and viral potency contradicts the disclosure; and it is not readily apparent from the claims how measurement of caspase-3 activity can be used to evaluate the stability of a virus. The rejection is respectfully traversed.

The present application under the heading of Summary of the Invention, and the Abstract, both indicate that viral induction of caspase 3 activity provides a measure of viral activity and can be used to measure viral stability and potency:

> Viral induction of caspase 3 activity was found to provide a reliable measure of viral activity. Assaying viral induction of caspase 3 activity can be used, for example, in methods for **measuring viral potency and stability**, and for evaluating the stability of a virus in different formulations. [Emphasis added.]

(Specification at page 1, lines 23-26, and the Abstract.)

The claims indicate measuring caspase 3 activity as an indication of virus activity. The greater the caspase 3 activity, the more viral activity present. If no caspase 3 activity is observed, the conclusion would be no viral activity. As increasing amounts of caspase 3 activity is observed, the conclusion would be more viral activity.

In addition, as noted above, claim 1 was amended to indicate using caspase 3 activity as an indication of viral activity to measure virus stability and potency in either: (i) different formulations; or (ii) a single formulation at two or more time intervals.

35 U.S.C. § 102 (Claims 1-3 and 7)

Claims 1-3 and 7 stand rejected as allegedly anticipated by Banki et al. (The Journal of Biological Chemistry May, 8, 1998; Vol 273, No. 19, 11944-11953.) The examiner argues Banki et al. teaches the same active steps as provided in claims 1-3 and 7. The rejection is respectfully traversed.

Claim 1 was amended to indicate using caspase 3 activity as an indication of viral activity to measure virus stability and potency in either: (i) different formulations; or (ii) a single formulation at two or more time intervals. In contrast, it is respectfully submitted that Banki et al. measures caspase 3 activity to study HIV induced apoptosis.

35 U.S.C. § 103 (Claims 4, 5, 18, 19)

Claims 4, 5, 18 and 19 stand rejected as allegedly obvious based on Banki et al. in view of Duncan et al. (Virology 255, 117-128, 1999). Duncan et al. is cited for teaching that the rubella virus induces apoptosis in Vero and RK13 cells, by quantifying the number of detached cells as an indicator of apoptosis. The examiner argues it would be prima facie obvious to use caspase 3 activity as an alternative measure of induced apoptosis. The rejection is respectfully traversed.

Duncan et al. concerns studying the cellular basis of the ability of the rubella virus to cause system birth defect in the fetuses of infected women. (See Duncan et al. abstract, first two sentences.) Duncan et al. indicates that other caspases, in addition to caspase 3, are involved the observed apoptosis. (Duncan et al., at 125, first column, 3rd paragraph.) Duncan et al., does not

indicate which other caspases to use in examining the cellular basis of the ability of the rubella virus to cause system birth defect in the fetuses of infected women.

It is respectfully submitted that the skilled artisan would not motivated to modify Duncan et al. to look at caspase 3 activity alone or in combination with other caspases. Rather, Duncan et al. teaches measuring apoptosis by quantifying detached cells.

Clams 4 and 5 further distinguish Banki et al. in combination with Duncan et al., based on the dependency to claim 1. Claim 1 was amended to indicate using caspase 3 activity as an indication of viral activity to measure virus stability and potency in either: (i) different formulations; or (ii) a single formulation at two or more time intervals.

35 U.S.C. § 103 (Claim 6)

Claim 6 stands rejected as allegedly obvious based on Banki et al., as applied to claims 1-3 in view of Wu et al. (provisional application 60/108606, priority document to U.S. Patent No. 6,689,600). Wu et al. is cited for teaching that lyophilization improves stability of viral vaccine and recombinant proteins. This rejection is respectfully traversed.

Claim 6 depends from claim 1. As noted above, claim 1 was amended to indicate using caspase 3 activity as an indication of viral activity to measure virus stability and potency in either: (i) different formulations; or (ii) a single formulation at two or more time intervals.

35 U.S.C. § 103 (Claim 8)

Claim 8 stand rejected as allegedly obvious based on Banki et al., as applied to claims 1-3 in view of Goodrich et al. (U.S. Patent No. 5958670). Goodrich et al. is cited for teaching a method of storing cells by freezing and later thawing. This rejection as respectfully traversed.

Claim 8 depends from claim 1. As noted above, claim 1 was amended to indicate using caspase 3 activity as an indication of viral activity to measure virus stability and potency in either: (i) different formulations; or (ii) a single formulation at two or more time intervals.

Please charge deposit account 13-2755 for fees due in connection with this response. If any time extensions are needed for the timely filing of the present response, applicant petition for such extensions and authorize the charging of deposit account 13-2755 for the appropriate fees.

Respectfully submitted,

By _____

Sheldon O. Heber
Reg. No. 38,179
Attorney for Applicant(s)

Merck & Co., Inc.
P.O. Box 2000
Rahway, New Jersey 07065-0907
(732) 594-1958